Remarks/Arguments

Claims 28-34, 37-39 and 42-53 are currently pending in the instant application. Claims 44 and 50-53 have been withdrawn. Claims 43 and 45 have been canceled. Claims 28, 46, and 48-49 have been amended. Claims 28-34, 37-39, 42, 43, and 47 have been rejected under 35 U.S.C. §112 first paragraph. Claim 43 has been rejected under 35 U.S.C. §112 second paragraph. Claims 28-34, 37-39, 42 and 47 have been rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,107,343 ("Sallmann"). Claims 28-34, 37-39, 42, 43 and 45-49 have been rejected under 35 U.S.C. §103(a) as being obvious over Sallmann in view of U.S. Patent No. 5,093,330 ("Caravatti"). Claims 28-33, 35-39, 42 and 47 have been rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,579,901 ("Chen") as evidenced by U.S. Patent No. 3,134,718 ("Nobile") in view of U.S. Patent No. 4,524,075 ("Oduro") and in further view of Shulin Ding, *Recent developments in Ophthalmic Drug Delivery*, 1 PSTT 328 (November 1998) ("Ding").

35 U.S.C. §112

The Examiner has rejected claims 28-34, 37-39, 42, 43, and 47 under 35 U.S.C. §112 first paragraph. In view of the amendment to claim 28, incorporating the limitations of claim 48 directed to particular types of staurosporine derivatives, Applicants respectfully submit that the instantly claimed invention satisfies the written description requirement.

The Examiner has rejected claim 43 under 35 U.S.C. §112 second paragraph. Claim 43 is now canceled. Accordingly, Applicants respectfully submit that this rejection is moot.

35 U.S.C. §103(a)

The Examiner has rejected claims 28-34, 37-39, 42 and 47 as obvious under 35 U.S.C. §103(a) in view of Sallmann. Sallmann does not disclose a compound of formula I. Accordingly, Applicant respectfully submits that the instantly claimed invention, as amended, is not obvious in view of Sallmann.

The Examiner has rejected claims 28-34, 37-39, 42, 43, and 45-49 as obvious under 25 U.S.C. §103(a) in view of Sallmann in further view of Caravatti. The Examiner alleges that Sallmann discloses an eye ointment for the delivery of opthalmically effective active agents containing phenylethyl alcohol as a preservative, cetylstearyl alcohol, liquid paraffin, white petrolatum and wool fat. The Examiner further alleges that Sallmann discloses that topical ophthalmic compositions can include solubilizers such as polyethylene glycols and polyethoxylated castor oils such as Cremophor EL and that PEG 400 is listed as one of the possible polyethylene glycols. The Examiner admits that Sallmann does not disclose the inclusion of staurosporine derivatives. The Examiner next alleges that Caravatti discloses the use of staurosporine derivatives in compositions for the treatment of diseases modulated by

protein kinase C, including use as an immunomodulator or anti-inflammatory. In the Examiner's view it would have been obvious to select the various disclose solubilizers and fillers from Sallmann and combine them with the staurosporine derivatives of Caravatti. The Examiner alleges that this is merely arranging old elements with each performing the same function it had been known to perform and yielding no more than one would expect from such an arrangement. Applicants respectfully disagree.

Applicants have discovered that compositions comprising staurosporine derivatives, an ointment base, and a poly(ethylene-glycol) exhibit good ocular tolerability properties. (*See* ¶¶[0134]-[0135] of the instant application). Sallmann discloses a group of possible solubilizers, including "tyloxapol, fatty acid glycerol poly-lower alkylene glycol esters, fatty acid poly-lower alkylene glycol esters, polyethylene glycols, glycerol, ethers" and mixtures of those compounds. (*See* Sallmann at c.4, ll.52-56). Moreover, Sallmann specifically identifies "an especially preferred solubilizer" namely, "a reaction product of castor oil and ethylene oxide" such as "Cremophor EL® or Cremophor RH 40®" and goes on to state that such products "have proven to be particularly good solubilizers that are tolerated extremely well by the eye." (*Id.* at c.4, ll.56-62). Additionally, Sallmann is focused primarily on eye drops. In the single example where Sallmann discloses an ophthalmic ointment (Example 7), Sallmann does not employ a polyethylene glycol; instead using tyloxapol which Sallmann discloses as "[a]nother preferred solubilizer". (*Id.* at c.4, l.62, c.9, ll.10-25).

Additionally, while Caravatti discloses staurosporine derivatives there is nothing in said reference which would suggest to one of ordinary skill in the art that said staurosporine derivatives should be combined with the teachings of Sallmann. Indeed, even if one were motivated to make such a combination one would be motivated to select either the "especially preferred solubilizer" or alternatively the other "preferred solubilizer"; i.e. a reaction product of castor oil and ethylene oxide or tyloxapol disclosed in Sallmann. (*Id.* at c.4, ll.56-62). This is especially true where the only disclosed ointment in Sallmann employs tyloxapol as the solubilizer. (*Id.* at c.9, ll.10-25). Accordingly, even if one were motivated to make the combination, one of ordinary skill in the art would not derive the claimed invention comprising a staurosporine derivative, an ointment base and a poly(ethylene-glycol) dispersing/dissolving agent. Additionally, neither Sallmann nor Caravatti suggest that combination of staurosporine derivative, ointment base and poly(ethylene-glycol) would exhibit good ocular tolerability properties. In view of the foregoing Applicant respectfully submits that the claimed invention is non-obvious.

The Examiner has rejected claims 28-34, 37-39, 42 and 47 as obvious under 25 U.S.C. §103(a) in view of Chen as evidenced by Nobile in further view of Oduro and in further view of Ding. The Examiner asserts that Chen discloses eye ointments comprising tacrolimus, anhydrous lanolin, liquid paraffin, vaseline, and HCO60. The Examiner admits that Chen does not disclose polyethylene glycol. The Examiner next alleges that Oduro discloses the use of

polyethylene glycols, such as PEG 400, for the formation of eye ointments or eye drops. The Examiner then alleges that Ding teaches that the use of viscosity enhancers is common in topical ophthalmic pharmaceuticals. In view of the amendment to claim 28, Applicants respectfully submit that this rejection is moot as none of the cited references disclose a staurosporine derivative of formula (I). Accordingly, a combination of the references fails to teach each element of the claimed invention and the invention is nonobvious.

In view of the foregoing, Applicants respectfully request withdrawal of the pending rejections and allowance of the instant application.

Respectfully submitted,

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